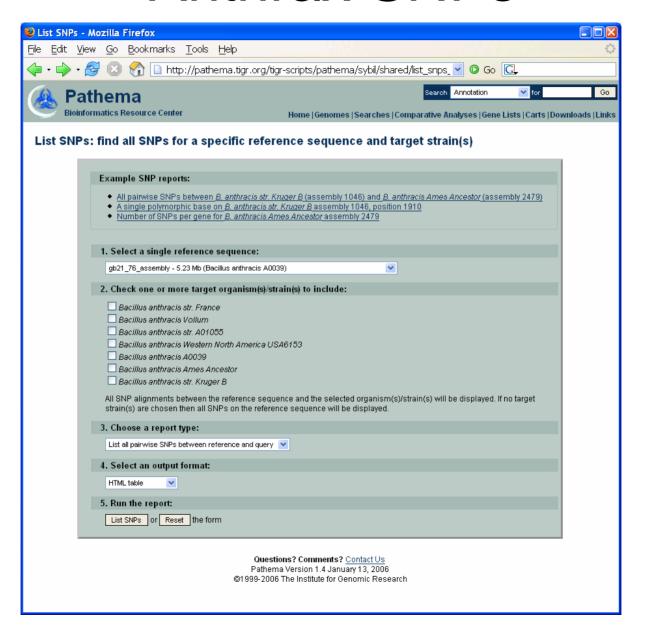
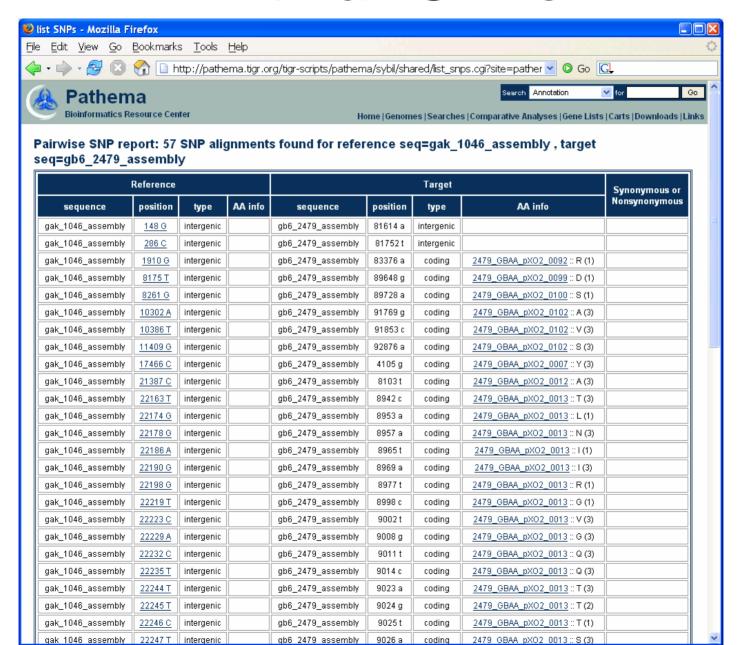
## Pathema Stuff

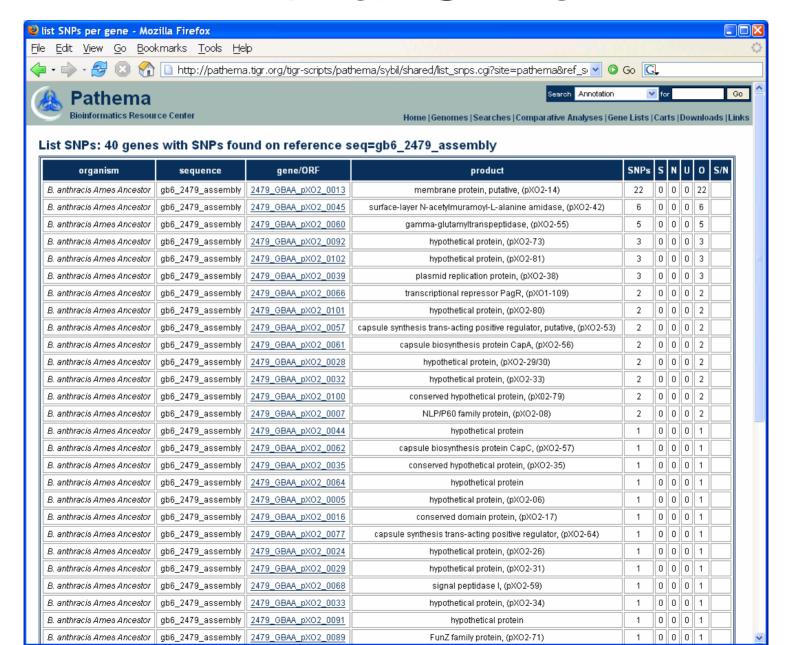
Feb 6<sup>th</sup>, 2006

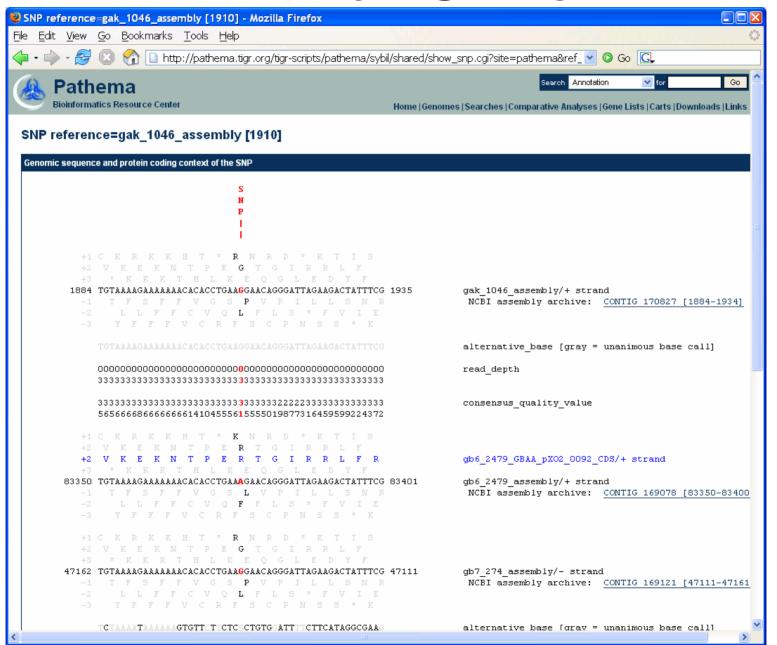


- Sequenced 7 B. anthracis strains
  - Including reference, Ames Ancestor, complete
- Load into Chado
- Employ mummer pipeline
- Identify polymorphic sites
- Curation at level of electropherogram
- → Total of 3,523 unique SNPs discovered





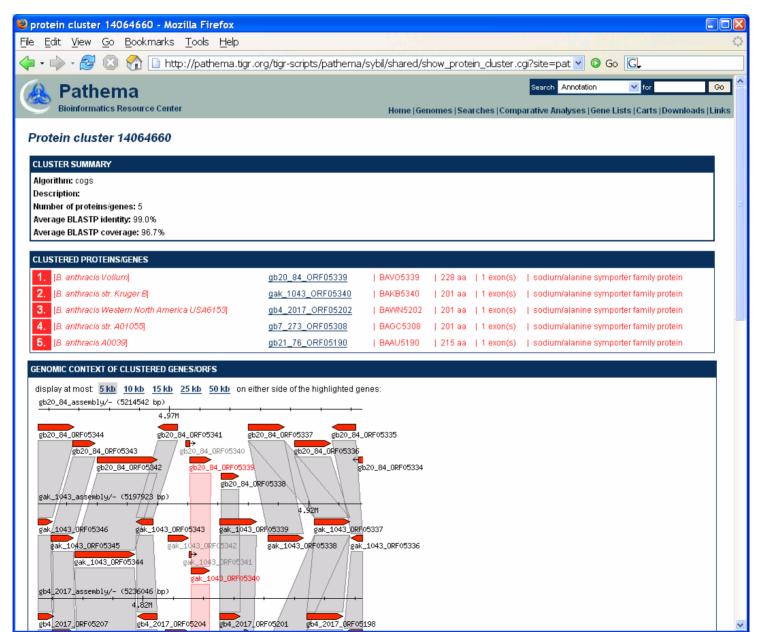




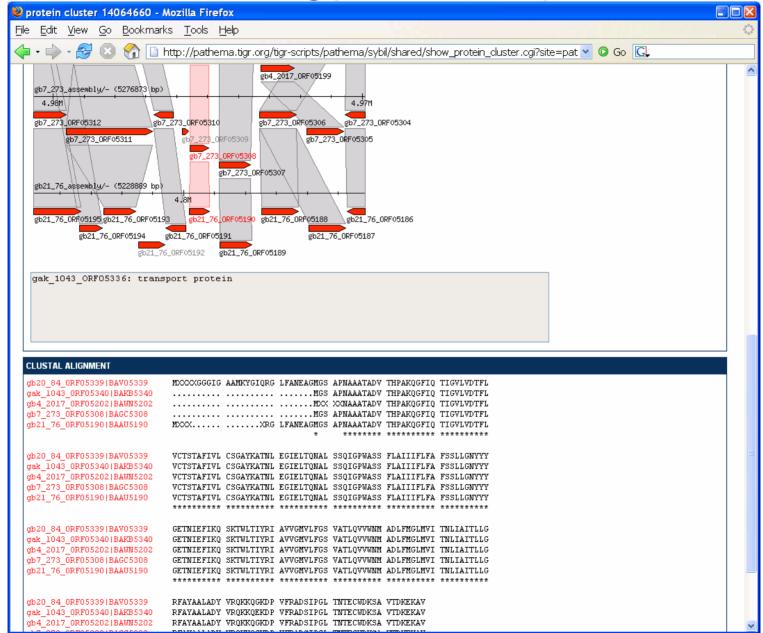
## Anthrax SNPs: Near future

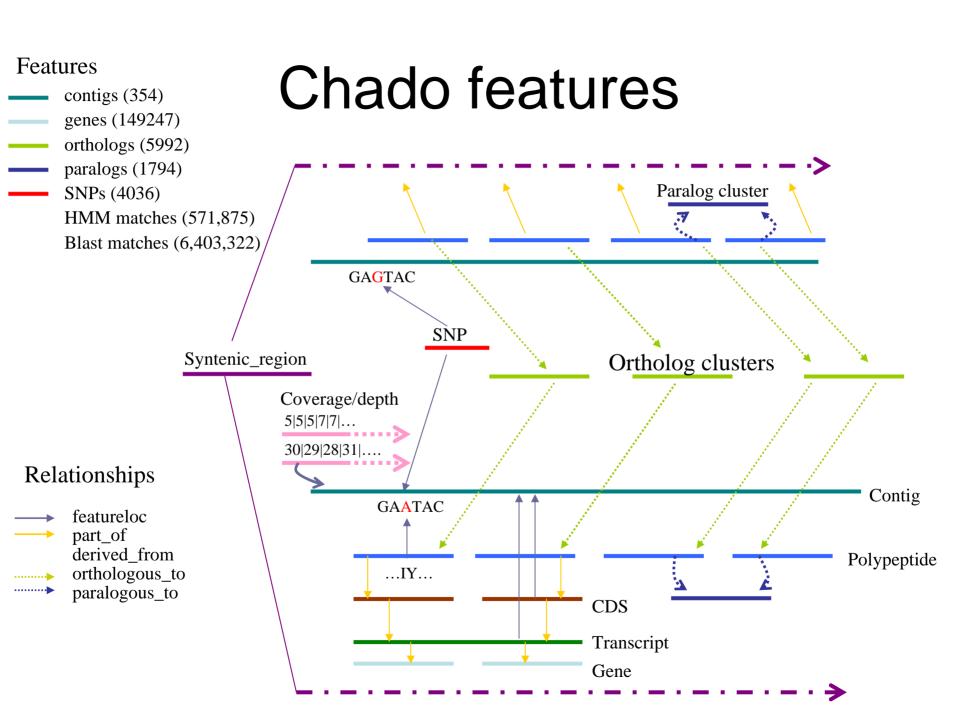
- Affymetrix resequencing chip
- 1,000 Anthrax strains
- Implications:
  - Performance?
  - Data model explosion?
  - Virtual sequence

# **Orthology Displays**



# **Orthology Displays**





## Reactions

Species	Genes	EC #s	Reactions	Pathways
B. Anthracis	1,619	656	943	75
B. Mallei	1,582	536	842	74
B. Pseudomallei	1,185	471	749	76
C. Botulinum	874	303	687	72
C. Perfringens	939	289	681	64



Pathways	Loci Names	EC numbers	Gene Names	
1- and 2-Methylnaphthalene degradation			acdS acyl-CoA dehydrogenase	Naphthyl-2-methyl-succ
1- and 2-Methylnaphthalene degradation			adh alcohol dehydrogenase	(2-Naphthyl)methanol +
1- and 2-Methylnaphthalene degradation			adh alcohol dehydrogenase	1-Hydroxymethylnaphth:
Alanine and aspartate metabolism			purB adenylosuccinate lyase	N6-(1,2-Dicarboxyethyl)-
Alanine and aspartate metabolism			purB adenylosuccinate lyase	N6-(1,2-Dicarboxyethyl)-
Aminoacyl-tRNA biosynthesis			serS serine-tRNA ligase	ATP + L-Serine + tRNA(
Aminoacyl-tRNA biosynthesis	CPE0014	6.1.1.11	serS serine-tRNA ligase	ATP + L-Serine + tRNA(
Aminoacyl-tRNA biosynthesis	CPE2464	6.1.1.14	glyS glycine-tRNA ligase	ATP + Glycine + tRNA(G
Aminoacyl-tRNA biosynthesis	CPE2464	6.1.1.14	glyS glycine-tRNA ligase	ATP + Glycine + tRNA(G
Aminophosphonate metabolism	CPE0071	2.7.8	clsA probable cardiolipin synthase	CMP-2-aminoethylphos
Aminophosphonate metabolism			clsA probable cardiolipin synthase	CMP-2-aminoethylphos
Aminophosphonate metabolism	CPE0365	2.7.8	clsB cardiolipin synthase	CMP-2-aminoethylphos
Aminophosphonate metabolism	CPE0365	2.7.8	clsB cardiolipin synthase	CMP-2-aminoethylphos
Aminophosphonate metabolism	CPE0711	2.6.1	aspC aspartate aminotransferase	3-Phosphonopyruvate +
Aminophosphonate metabolism	CPE0754	2.7.8	clsC cardiolipin synthase	CMP-2-aminoethylphos
Aminophosphonate metabolism	CPE0754	2.7.8	clsC cardiolipin synthase	CMP-2-aminoethylphos
Aminophosphonate metabolism	CPE0854	2.6.1	aspC aspartate transaminase	3-Phosphonopyruvate +
Aminosugars metabolism	CPE0075		PTS	UDP-N-acetylmuramate
Aminosugars metabolism	CPE0076		PTS	UDP-N-acetylmuramate
Aminosugars metabolism	CPE0077		PTS	UDP-N-acetylmuramate
Aminosugars metabolism	CPE0154		probable	UDP-N-acetylmuramate
Aminosugars metabolism	CPE0184	5.1.3.9	nanP putative N-acylglucosamine-6-phosphate 2-epimerase	N-Acetyl-D-glucosamine
Aminosugars metabolism	CPE0185	4.1.3.3	nanA acylneuraminate lyase	N-Acetylneuraminate <=
Aminosugars metabolism	CPE0266		probable	UDP-N-acetylmuramate
Aminosugars metabolism	CPE0353	1.1.1.158	murB UDP-N-acetylenolpyruvoylglucosamine reductase	UDP-N-acetylmuramate
Aminosugars metabolism	CPE0981		probable	UDP-N-acetylmuramate
Aminosugars metabolism	CPE1364		beta-N-acetylhexosaminidase	UDP-N-acetylmuramate
Aminosugars metabolism	CPE1992		probable	UDP-N-acetylmuramate
Aminosugars metabolism	CPE2131	3.1.4	rng ribonuclease G	N-Acetyl-D-mannosamii
Aminosugars metabolism	CPE2176	3.5.1.25	nagA N-acetylglucosamine-6-phosphate deacetylase	N-Acetyl-D-glucosamine
Aminosugars metabolism	CPE2196		UDP-N-acetylglucosamine	UDP-N-acetylmuramate
Aminosugars metabolism	CPE2329		phosphoglucosamine	UDP-N-acetylmuramate
Aminosugars metabolism	CPE2434	3.5.99.6	nagB glucosamine-6-phosphate isomerase	D-Glucosamine 6-phos
Aminosugars metabolism	CPE2490		glucosamine-1-phosphate	UDP-N-acetylmuramate
Arginine and proline metabolism	CPE0150		2-dehydro-3-deoxyphosphogluconate/4-hydroxy-2-ox	L-Proline + NAD+ <=> (8
Arginine and proline metabolism	CPE0150		2-dehydro-3-deoxyphosphogluconate/4-hydroxy-2-ox	trans-4-Hydroxy-L-prolin
Arginine and proline metabolism	CPE0256		probable	L-Proline + NAD+ <=> (8
Arginine and proline metabolism	CPE0256		probable	trans-4-Hydroxy-L-prolin
Arginine and proline metabolism	CPE0551	3.5.3.11	speB probable agmatinase	Agmatine + H2O <=> Pu
Arginine and proline metabolism	CPE0757		creatinase	L-Proline + NAD+ <=> (§
Arginine and proline metabolism	CPE0757		creatinase	L-Proline + NAD+ <=> (8
Arginine and proline metabolism	CPE0757		creatinase	trans-4-Hydroxy-L-prolin
Arginine and proline metabolism	CPE1050		5'-methylthioadenosine/S-adenosylhon beysteine	Proline + NAD+ <=> (8
Arginine and proline metabolism	CPE1050		5'-methylthioadenosine/S-adenosylhon ocysteine	trans-4-Hydroxy-L-prolin
Arginine and proline metabolism	CPE1670		acnC achartate transaminace	I anthro 4 Hydroxyaluta
2			reactome.org	, , ,

reactome.org \( \)

# Genome Properties

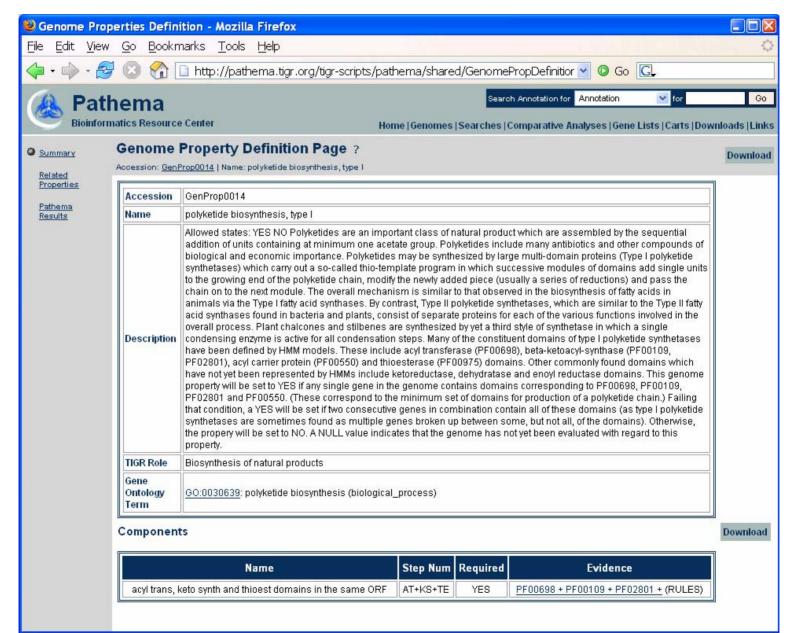
Project	Biochemica I Pathways	Protein Transport	Small Molecule Transport	Non- transport
B. anthracis Ames	53 (5)	3 (0)	6 (2)	47 (10)
B. mallei	65 (11)	6 (2)	7 (2)	58 (9)
B. pseudomallei	66 (11)	7 (3)	8 (1)	66 (14)
C. botulinum	35 (10)	4 (0)	5 (1)	46 (12)
C. perfringens	35 (13)	2 (1)	4 (2)	45 (9)

Properties with partial evidence are counted as positive assertions and denoted in parentheses.

Assessment of 85 biochemical pathways and 19 specific transport networks

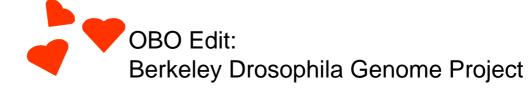
Genome Properties: a system for the investigation of prokaryotic content. Bioinformatics. 2005 Feb 1;21(3):293-306.

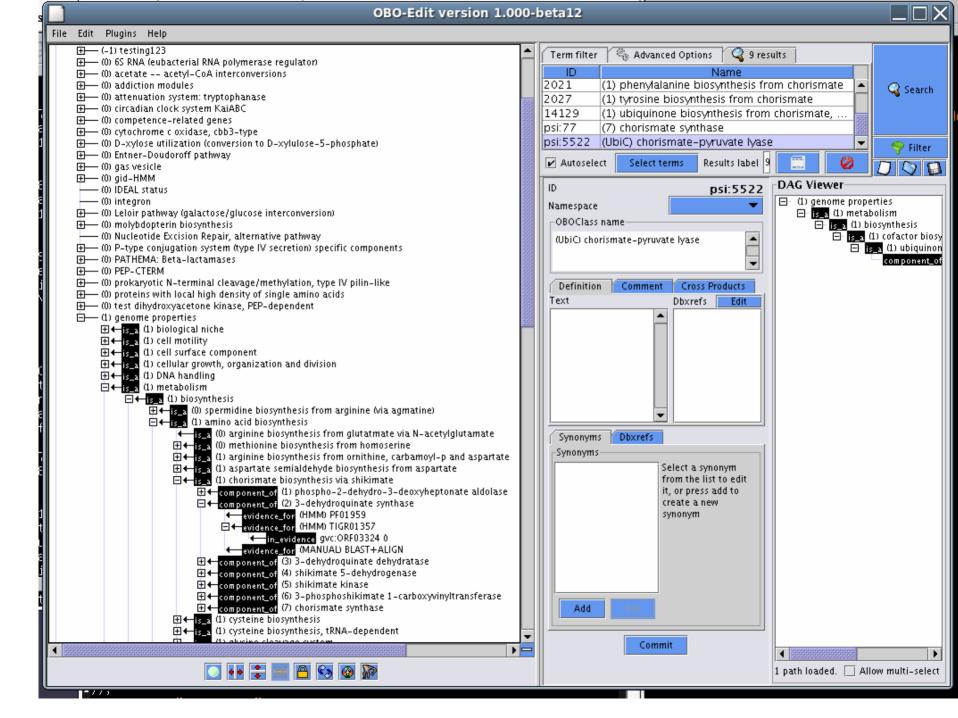
# Genome Properties



## **OBO Edit Usage**

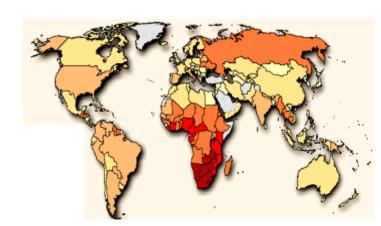
- Properties have parent-child relationship
- Components are children of property
- Evidence is child of component
- Genes found by evidence are children of evidence
- Load those relationships into OBO edit...
- Exchange format for GP?





# Epidemiological data

- With more and more strains being sequenced we need to be able to correlate new data-types with sequence information....eg ...
  - Geographical information (country, city or GPS)
  - Clinical symptoms
  - Date of isolation
  - Host range (organism taxon, sex, age, etc)
  - Tissue/cell type that is infected
  - Method of transmission
  - reservoir
  - etc, etc ,etc



reservoir

### Microbial Rosetta Stone Database

The Microbial Rosetta Stone Database: a compilation of global and emerging infectious microorganisms and bioterrorist threat agents.

Ecker DJ, Sampath R, Willett P, Wyatt JR, Samant V, Massire C, Hall TA, Hari K, McNeil JA, Buchen-Osmond C, Budowle B.

BMC Microbiol. 2005 Apr 25;5(1):19.

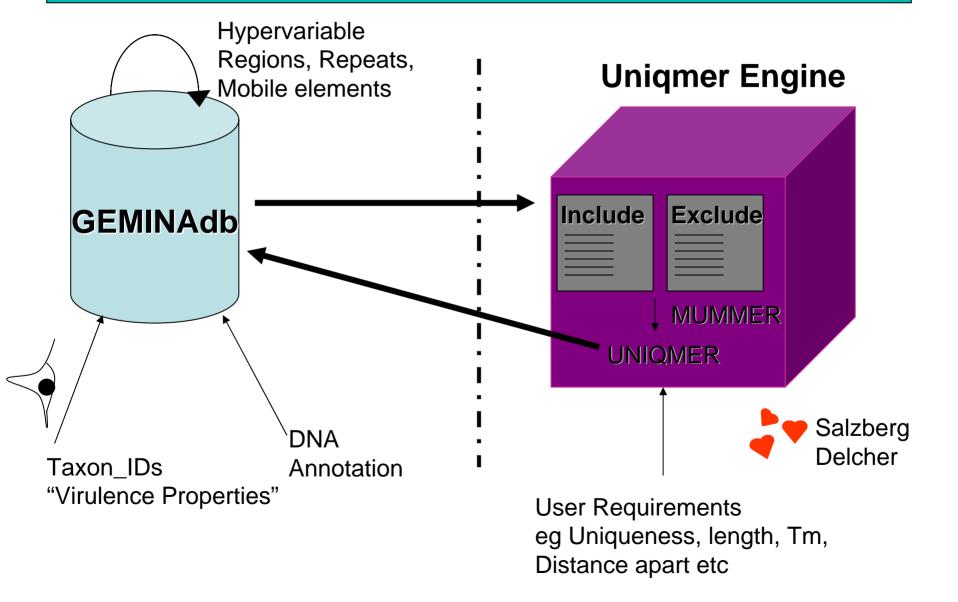
Ibis Therapeutics



## The Gemina database

- Fully relational
- Highly research-brittle
- IP agreements in progress
- Content
  - Protocols
  - Taxon → epi data
  - Hierarchically structured CVs:
    - anatomy, disease, symptom, transmission method, reservoir, geographic location
- Example queries:
  - "all of the DNA sequences of pathogens that infect the gut"
  - "all of the the airborne pathogens found in the USA"
  - "All the flu viruses isolated in 2005"

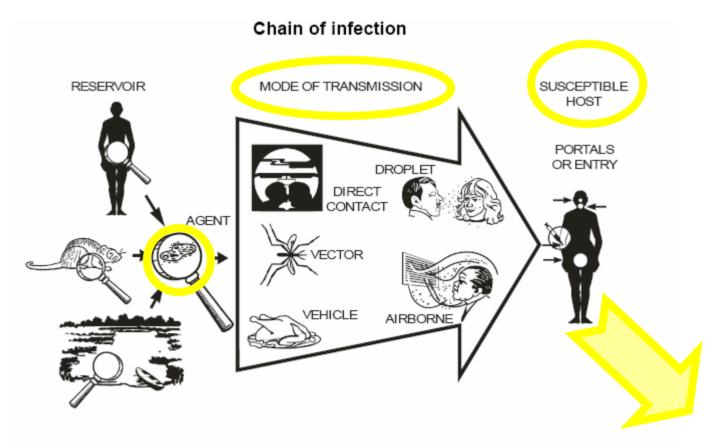
# The DNA signature pipeline

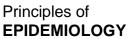


# Infection Systems: representation of the "Chain of Infection"

Pathogen -- Component -- Host -- Disease

Bacillus anthracis str. Ames – Skin – Human - Anthrax Bacillus anthracis str. Ames Ancestor – Respiratory Tract – Cow - Anthrax





U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Centers for Disease Control and Prevention (CDC)



### **Ontologies & Controlled Vocabularies In Gemina**

- infectious disease and body system oriented
- hierarchical query and retrieval

anatomy — disease — symptom <u>— transmission\_method —</u> reservoir — geographic location





- → FlyBase controlled vocabulary
- → MESH
- → NCI Thesaurus





#### disease

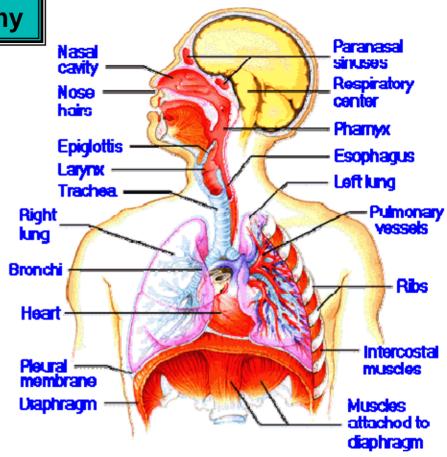
- +diseases of the respiratory system
- +infectious and parasitic diseases
  - +arthropod-borne viral disease
  - +intestinal infectious diseases
    - +other bacterial diseases
      - +bacterial infection
        - +gas gangrene
        - +staphylococcus infection
        - +tetanus

#### reservoir

- +animal reservoir
  - +arthropod
  - +mollusc
- +environmental reservoir
  - +soil
  - +food
- +human reservoir
  - +blood
  - +respiratory tract

### **Components -- Tissues -- Anatomy**

- +Animal\_structure
- +Body\_region
- +Cardiovascular\_system
- +Cell
- +Digestive\_system
- **+Embryonic\_structure**
- +Endocrine\_system
- +Fluids\_and\_secretions
- **+**Hemic\_and\_immune\_system
- +Integumentary\_system
- +Musculoskeletal\_system
- +Nervous\_system
- +Respiratory\_system
- +Sense\_organ
- +Stomatognathic\_system
- **+**Tissue
- +Urogenital\_system

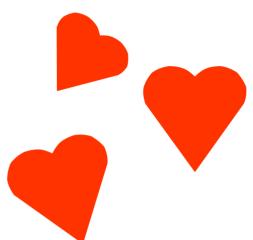


### Respiratory\_system

- + larynx
- + lung
- + pharynx
  - + nasopharynx
  - + oropharynx

## epidemiology CVs sources

- Mesh files at OBO:
  - anatomy (tissue component)
  - symptom
  - geographical location
- Rat Genome Database
  - disease → divided this into separate ontologies
    - diseases and symptoms.
- literature, web sites and epidemiology sources
  - transmission method
  - reservoir ontologies



## anatomy ontology (1,318)

- pared down ontology to describe
  - body parts
  - body systems
  - body components
- augmenting with specific human cell types.

## disease ontology (402)

- augmented
  - infectious disease
  - mycoses
  - zoonoses
- removed non-infectious conditions/diseases (e.g., congenital conditions).
- separated out symptom into separate ontology
- augmented this ontology with ICD-10 data the WHO

# symptom ontology (254)

- began at signs and symptoms node
- organized the symptoms ontology to match disease ontology
- separated:
  - General symptoms, v.
  - Symptoms involving the various body regions or systems

# geographical location (370)

- extracted from MeSH
  - defined the children of regions
  - includes additional nodes where needed (e.g., city/county)
  - added US Census
  - added CIA list of countries

## transmission method (11)

- curated transmission mode from Principles of Epidemiology, from CDC
  - direct modes
    - Kissing, skin-to-skin, contact w/ soil
  - indirect modes
    - Airborne
    - Vehicle borne, medical (tissue transplant)
    - Vector borne (flea bite)



## natural reservoir (81)

- created top nodes:
  - Environmental
  - Human
  - Animal
- added
  - literature
  - web sites
  - epidemiology sources.

## infection systems

anatomy - disease - symptom - transmission method - reservoir - geographic location

- Species (10)
  - Bacillus anthracis, Bacillus anthracis Ames,
     Bacillus anthracis Ames Ancestor,
     Bacillus anthracis Sterne (11)
  - Brucella spp, B. melitensis, B. abortus, B. suis, B. canis (85)
  - Burkholderia mallei: (29)
- Current total: 135
- Underway: Human and avian flu



## Obligate Collaborations

- Anthrax SNPs: Jaques Ravel@tigr
- Chado: FlyBase and BDGP.
- Mummer/SNP/Signature: Salzberg@UMd
- Reactome: CSHL, EBI, GO<sup>tm</sup>
- Gene function CV: GO<sup>tm</sup> consortium
- MRS database: Ibis Therapeutics